JACC Vol. 29, No. 7
June 1997:1549–56

Coronary Calcification and Coronary Atherosclerosis: Site by Site Comparative Morphologic Study of Electron Beam Computed Tomography and Coronary Angiography

KOUJI KAJINAMI, MD,*† HIROYASU SEKI, MD,† NOBORU TAKEKOSHI, MD,† HIROSHI MABUCHI, MD*

Kanazawa, Japan

Objectives. **We compared, on a site by site basis, the morphologic features of coronary calcifications determined by electron beam computed tomography (EBCT) and angiographically defined coronary atherosclerosis.**

Background. **Quantification of coronary calcification using EBCT is clinically useful for the prediction of coronary stenosis. However, the relation between calcification and angiographic findings has not been evaluated by site.**

Methods. **We studied 251 consecutive patients who underwent elective coronary angiography for suspected coronary artery disease by EBCT and analyzed findings by site. Coronary calcifications were classified according to their length and width versus the diameter of the coronary artery in which the calcification was observed as: none, spotty, long, wide and diffuse.**

Results. **Coronary calcifications were found in 666 (27%) of 2,470 segments. The positive predictive value (PPV) of coronary calcification for significant stenosis (≥75% densitometric narrowing) and for all angiographically detectable atherosclerotic lesions in a segment was 0.36 and 0.80, respectively. The PPV for significant stenosis and all atherosclerotic lesions was 0.04 and 0.17 in none, 0.18 and 0.59 in spotty, 0.32 and 0.87 in long, 0.40 and 0.84 in wide and 0.56 and 0.96 in diffuse calcifications, respectively. The PPV for both significant stenosis and all lesions differed significantly (p = 0.001) among the morphologic groups. Of the 105 eccentric significant stenoses, 54 (53%) were classified as long or diffuse calcifications. Of the 95 significant stenoses with multiple irregularities, 61 (64%) showed diffuse calcification.**

Conclusions. **Morphologic evaluation of coronary calcifications using EBCT improved the prediction of coronary stenosis on a site by site basis and provided information related to angiographic morphology.**

(J Am Coll Cardiol 1997;29:1549–56)

The presence of coronary calcifications in the intima of the vessel wall is invariably associated with atherosclerotic plaque (1–3). Quantification of the total amount of coronary calcification by electron beam computed tomography (EBCT) (4), which is more sensitive than previously used methods such as fluoroscopy (5), is useful for predicting clinically significant coronary artery disease (6–18) as well as future cardiovascular events (19,20). However, studies comparing pathologic and EBCT findings have shown (21–26) that the degree of lumen narrowing is weakly correlated with the amount of calcification and thus may vary widely, even at sites with a similar degree of calcification. The relation between the coronary calcification detected by EBCT and the angiographically determined degree of lumen narrowing has not been studied on a lesion by lesion or a site by site basis in the clinical setting.

A compensatory enlargement of the coronary artery is a widely recognized phenomenon (27) that results in false negative or underestimated angiographic results, even when a substantial amount of atherosclerotic plaque is present in the arterial wall. This phenomenon also suggests that the clinical significance of the cross-sectional and longitudinal extent of atheromatous plaque in the vessel wall may differ. If so, this difference may also be applicable to coronary calcification.

In the present study, we compared the results of EBCT detection of coronary artery calcification and coronary angiography on a site by site basis, with emphasis on the morphologic characteristics.

Methods

Study patients. We prospectively studied 251 consecutive Japanese patients (174 men, 77 women; mean [± SD] age 56 ± 14 years, range 16 to 86) who underwent elective coronary angiography between May 1991 and May 1993. Excluded were patients in unstable condition and those who had undergone previous coronary interventional procedures, such as bypass

From the *Second Department of Internal Medicine, School of Medicine, Kanazawa University and †Kanazawa Cardiovascular Hospital, Kanazawa, Japan. This work was presented in part at the 43rd Annual Scientific Session of the American College of Cardiology, Atlanta, Georgia, March 1994.

Manuscript received September 30, 1996; revised manuscript received January 31, 1997, accepted February 26, 1997.

Address for correspondence: Dr. Kouji Kajinami, The Second Department of Internal Medicine, School of Medicine, Kanazawa University, Takara-machi 13-1, Kanazawa 920, Japan. E-mail: athero@med.kanazawa-u.ac.jp.

Published by Elsevier Science Inc.

0735-1097/97/$17.00
PII S0735-1097(97)00090-9

Abbreviations and Acronyms

AHA	=	American Heart Association
EBCT	=	electron beam computed tomography (tomographic)
ECG	=	electrocardiographic
LAD	=	left anterior descending coronary artery
LAO	=	left anterior oblique
LCx	=	left circumflex coronary artery
NPV	=	negative predictive value
PPV	=	positive predictive value
RAO	=	right anterior oblique
RCA	=	right coronary artery

surgery or angioplasty. Patients with abnormal Q waves in two or more electrocardiographic (ECG) leads were also excluded because they were presumed to have coronary artery disease. Thus, the study included patients who 1) presented with chest pain (induced by effort or occurring at rest, or both) suggesting angina pectoris; or 2) had ECG findings at rest that indicated possible myocardial ischemia. The EBCT study was performed within 2 weeks of angiography in most patients and in all but 12. EBCT was performed in the last 2 to 4 weeks before or after angiography. Informed consent was obtained from all patients before the examinations. The present study cohort is the same patient group in which we previously investigated the usefulness of the total coronary calcification score for prediction of angiographically confirmed coronary atherosclerosis (17).

Scanning protocol, image analysis and definition of coronary artery segments on EBCT images. EBCT studies were performed using the volume mode (100-ms scan time) of the Imatron C-100 scanner, as previously described (17,28). We obtained 20 contiguous 3-mm thick slices through the base of the heart. Additional slices were obtained to cover the entire coronary artery tree. The procedure was repeated within a few minutes after patients were repositioned on the couch. Images were evaluated by an experienced observer without knowledge of the clinical data or the angiographic results. The analysis was confirmed by a cardiologist and a radiologist in a subsequent weekly conference, again without knowledge of the clinical or angiographic data. A *calcified lesion* was defined as a lesion with an EBCT density ≥130 and an area ≥0.51 mm^2 (2 pixels). Coronary segments were identified on EBCT images as illustrated in Figure 1.

Calcifications were classified morphologically as none, spotty, long, wide and diffuse on the basis of the width (extent of the calcification perpendicular to the longitudinal direction of the vessel) and length (extent in the longitudinal direction of the vessel) of the calcification in relation to the coronary artery diameter in the area where calcification was observed (Table 1). A segment with more than three calcifications was classified as the *diffuse type*. If two scans resulted in different morphologic classifications of the segment, we used the scan showing the larger amount of calcification in that segment.

Coronary angiography. Elective coronary angiography was performed in multiple projections using the standard tech-

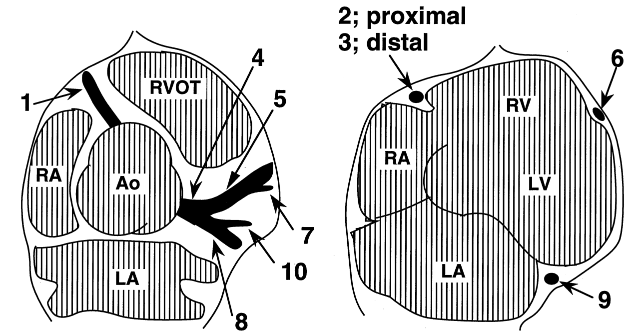


Figure 1. Identification of coronary artery segments on EBCT images. Segment 1 (S-1) was the proximal portion of the RCA, usually running in a horizontal plane. The portion that descended into the right atrioventricular groove in a caudal direction was divided into two halves, with the proximal portion defined as S-2 and the distal portion as S-3. The distal portions of the RCA on the diaphragmatic surface of the heart were not analyzed. S-4 was the main trunk of the left main coronary artery. The proximal portion of the LAD running in a horizontal plane was S-5. The proximal half of the LAD located in the anterior intraventricular groove was S-6. The largest diagonal branch was S-7. The proximal portion of the LCx running toward the obtuse margin was S-8. That part of the LCx running in the left atrioventricular groove in a caudal direction was S-9. The major branch of the LCx was S-10. Ao = ascending aorta; LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle; RVOT = right ventricular outflow tract.

nique. Angiograms were reviewed by several experienced staff cardiologists who were unaware of the results of the computed tomographic study and the clinical data. The extent of coronary artery stenosis was measured by computer-assisted videodensitometry with the use of a CCIP-310 (Cathex Inc., Tokyo, Japan), as previously described (17). *Significant coronary artery stenosis* was defined as ≥75% densitometric narrowing. *Mild stenosis* was defined as an angiographically detectable lesion with <75% densitometric narrowing. Angiographic lesions were classified morphologically as *concentric*, *eccentric type 1*, *eccentric type 2* and *multiple irregularities*, according to the criteria reported by Ambrose et al. (29) for significant and mild stenoses.

Site by site lesion comparison. Angiographic segments were identified with reference to the method for determination of coronary segments on EBCT images. S-1 and S-2 were

Table 1. Classification of Coronary Calcifications Observed on Electron Beam Computed Tomographic Images

Calcification Morphology	Lesion Width*	Lesion Length†
Diffuse	≥2/3 of coronary diam	≥3/2 coronary diam
Wide	≥2/3 of coronary diam	<3/2 coronary diam
Long	<2/3 of coronary diam	≥3/2 coronary diam
Spotty	<2/3 of coronary diam	<3/2 coronary diam
None	Undetectable	Undetectable

*Extent of calcification perpendicular to the longitudinal direction of the vessel. †Extent of lesion in the longitudinal direction of the vessel. diam = diameter.

defined as the opposite sides of the point at which the right coronary artery (RCA) turns in a caudal direction on the left anterior oblique (LAO) view. The point at which the RCA again turns in a horizontal direction (the acute margin) indicates the termination of S-3. The distal end of S-5 was defined as the turning point of the left anterior descending coronary artery (LAD) from a nearly horizontal to an antero-caudal direction on the right anterior oblique (RAO) view. The distal end of S-8 was defined as the angle (the obtuse margin) of the left circumflex coronary artery (LCx) on the LAO view with cranial angulation. Definitions of S-7 and S-10 were difficult in some cases because the most proximal branches of the LAD and LCx were not always the largest ones. Thus, in 10 patients, the tomographic segment was first identified and then confirmed on angiography. The angiographic classification system used in the present study is similar to the American Heart Association (AHA) classification system (30). However, the "proximal RCA" (No. 1) in the AHA system is divided into S-1 and S-2 in the present study. If a calcification on EBCT images and an angiographic lesion were located over two or more adjacent segments, we compared the characteristics of each segment after the lesion was separated into segments according to the method described (Fig. 1). Some examples of lesion comparison between EBCT images and angiography are shown in Figure 2.

Statistical analysis. The ability of coronary calcification to predict angiographically defined coronary atherosclerosis was evaluated by calculating the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy. Differences in PPVs among the calcification morphology groups were analyzed using 2×4 or 2×5 tables and the chi-square test with 3 or 4 degrees of freedom, respectively. A p value <0.05 was accepted as indicating statistical significance.

Results

Detection of calcifications. Of the 2,510 segments studied, we excluded 40 from analysis for the following reasons: Total occlusion of the coronary artery prevented angiographic visualization in 30 segments; 2 branches of the LAD (S-7) and 2 of the LCx (S-10) observed on angiography could not be identified on tomographic images; and the RCA and LCx were too small to permit comparison in 6 segments (S-3, n = 5 and S-9, n = 1). Calcifications were detected in 666 (27%) of the 2,470 segments analyzed (Table 2). The diffuse and spotty types of calcification were observed with similar frequency; the wide type was the least common. Calcifications were most common in the proximal LAD (S-5) and least common in the major branch of the LCx (S-10).

Prediction of coronary stenosis by calcification. The PPVs of coronary calcification for prediction of significant stenosis and all atherosclerotic lesions were 0.36 and 0.80, respectively. On the basis of comparison among five subgroups (<40, $40 \leq 50$, $50 \leq 60$, $60 \leq 70$ and ≥ 70 years) both the PPV and NPV for significant stenosis did not change with age (0.25 to 0.40 and 0.94 to 1.00, respectively). By contrast, both the specificity and accuracy decreased with age (0.97 to 0.72 and 0.97 to 0.73, respectively). The PPV and the sensitivity increased with age for all atherosclerotic lesions (0.33 to 0.86 and 0.18 to 0.69, respectively), whereas the specificity, NPV and accuracy decreased slightly with age (0.97 to 0.90, 0.94 to 0.77 and 0.92 to 0.80, respectively).

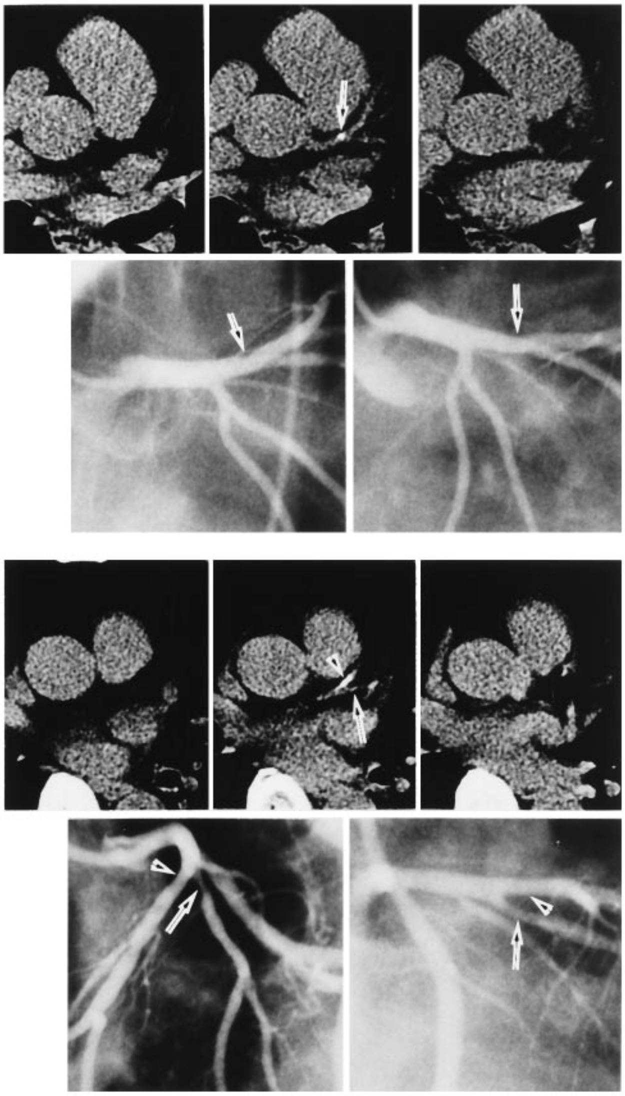


Figure 2. EBCT and coronary angiographic images of lesions in two representative patients. **Upper panels**, Spotty calcification was detected in the proximal LAD (S-5) on the EBCT image (**arrow**) in a 59-year old man. A mild eccentric lesion was observed on the angiograms (**arrows**). **Lower panels**, Diffuse calcification was observed in the proximal LAD (S-5) (**arrowhead**) and wide calcification in the diagonal branch (S-7) (**arrow**) in a 66-year old man. Angiography demonstrated a mild eccentric lesion (**arrowheads**) and significant concentric stenosis (**arrows**).

Calcifications in the left main (S-4) and proximal LAD (S-5) segments showed the highest sensitivity for all atherosclerotic lesions (Table 3). For prediction of significant stenosis, the validity was similar in all of 10 segments (Table 4). We separated the patient group by gender and performed a similar

Table 2. Morphologic Classification of Segments With Calcification

	Coronary Segment									
	RCA				LAD			LCx		
Morphology (total no. of segments)	S-1	S-2	S-3	LMCA: S-4	S-5	S-6	S-7	S-8	S-9	S-10
Diffuse (n = 230)	23	30	15	14	45	33	25	21	18	6
Wide (n = 57)	2	3	4	8	7	9	2	9	9	4
Long (n = 142)	17	26	13	15	39	7	2	11	9	3
Spotty (n = 227)	26	32	10	26	33	25	23	30	18	4
All calcification (n = 656)	68	91	42	63	124	74	52	71	54	17
None (n = 1,814)	180	155	195	188	122	171	197	178	196	232
Total (n = 2,470)	248	246	237	251	246	245	249	249	250	249

LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; LMCA = left main coronary artery; RCA = right coronary artery.

analysis. However, no significant gender difference could be found for any variable (data not shown). After the exclusion of spotty type from significant calcification, the specificity and the PPV increased, and the sensitivity and the NPV decreased, respectively (Tables 3 and 4).

Morphology of calcification and prediction of stenosis. The PPV for morphologic subgroups for both significant stenosis and all atherosclerotic lesions differed significantly ($p = 0.0001$ to 0.0069) in all age groups, except for the <40-year old group (Tables 5 and 6). For all significant stenoses, the PPV increased in the following sequence: none, spotty, long, wide and diffuse; and decreased with age for diffuse and wide calcifications and increased with age for long and spotty calcifications. For all atherosclerotic lesions, the PPV of spotty calcification increased with age, whereas that for diffuse, wide and long calcifications remained constant. There was no significant difference when a similar analysis was performed after the patient group was separated by gender (data not shown). To investigate the relation between the morphology and amount of calcification, we calculated the mean calcified area in S-5, for example. Mean calcified area was smallest in spotty calcifications (6.5 mm^2); similar in long and wide calcifications (22.7 and 21.3 mm^2, respectively) but significantly larger than that of spotty calcifications; and largest in diffuse calcifications (75.4 mm^2), with significant overlap with both long and wide calcifications.

Sensitivities and specificities were recalculated after calcification morphology and total coronary calcification scores were combined, as previously reported (17). In patients with a score higher than the cutoff level (log-transformed score 3.0), detection of any calcification could predict significant stenoses and all atherosclerotic lesions with a sensitivity of 0.82 and 0.74 and a specificity of 0.61 and 0.85, respectively. For scores lower than the cutoff level, detection of calcification had a sensitivity of 0.32 and 0.47 and a sensitivity of 0.94 and 0.95, respectively.

Morphologic comparison of EBCT images and angiographic findings. Diffuse calcification was strongly associated with significant stenosis (PPV 0.56), especially stenoses classified as having multiple irregularities (61 of 127 significant stenoses showed multiple irregularities) (Fig. 3). Of the 23 concentric lesions with significant stenosis, 13 (57%) were associated with wide calcification; the frequencies of the other morphologic classifications ranged from 22% to 43%. When we analyzed the relation between EBCT calcification morphology and angiographic lesion morphology, we found that 61 (64%) of 95 multiple irregular lesions showed diffuse calcifi-

Table 3. Prediction of All Coronary Atherosclerotic Lesions by Calcification According to Segment*

Segment†	No.	Sens	Spec	PPV	NPV	Accuracy
S-1	248	0.57/0.40	0.90/0.97	0.78/0.88	0.78/0.73	0.78/0.75
S-2	246	0.61/0.47	0.86/0.98	0.81/0.97	0.70/0.70	0.74/0.74
S-3	237	0.55/0.42	0.96/0.97	0.83/0.84	0.85/0.82	0.85/0.82
S-4	251	0.92/0.63	0.91/0.97	0.71/0.84	0.98/0.92	0.91/0.90
S-5	246	0.84/0.66	0.89/0.97	0.90/0.97	0.83/0.71	0.87/0.80
S-6	245	0.51/0.42	0.87/0.99	0.77/0.96	0.68/0.67	0.71/0.73
S-7	249	0.63/0.38	0.94/0.97	0.77/0.83	0.88/0.82	0.86/0.82
S-8	249	0.61/0.44	0.88/0.98	0.73/0.90	0.81/0.77	0.79/0.79
S-9	250	0.61/0.45	0.94/0.98	0.80/0.89	0.86/0.82	0.84/0.83
S-10	249	0.29/0.23	0.99/0.99	0.82/0.85	0.85/0.84	0.85/0.84
All	2,470	0.63/0.47	0.92/0.98	0.80/0.91	0.83/0.78	0.82/0.80

*All values were obtained when all four calcification morphologies were significant/when only three morphologies (long, wide and diffuse) were significant. †See Figure 1 and text. NPV = negative predictive value; PPV = positive predictive value; Sens = sensitivity; Spec = specificity.

Table 4. Prediction of Significant Coronary Stenosis by Calcification According to Segment*

Segment†	No.	Sens	Spec	PPV	NPV	Accuracy
S-1	248	0.84/0.72	0.79/0.89	0.31/0.43	0.98/0.97	0.79/0.88
S-2	246	0.89/0.81	0.69/0.83	0.26/0.37	0.98/0.97	0.72/0.83
S-3	237	0.90/0.70	0.85/0.89	0.21/0.22	0.99/0.99	0.86/0.88
S-4	251	0.93/0.80	0.79/0.89	0.22/0.24	0.99/0.99	0.80/0.88
S-5	246	0.93/0.84	0.64/0.78	0.46/0.56	0.97/0.94	0.71/0.80
S-6	245	0.72/0.58	0.81/0.91	0.51/0.63	0.91/0.89	0.79/0.84
S-7	249	0.65/0.38	0.87/0.93	0.46/0.48	0.93/0.90	0.84/0.85
S-8	249	0.79/0.79	0.78/0.91	0.32/0.55	0.97/0.97	0.78/0.90
S-9	250	0.65/0.50	0.85/0.91	0.41/0.47	0.94/0.92	0.82/0.86
S-10	249	0.40/0.30	0.98/0.98	0.71/0.69	0.92/0.91	0.91/0.90
All	2,470	0.75/0.63	0.81/0.89	0.36/0.46	0.96/0.94	0.80/0.86

*All values were obtained when all four calcification morphologies were significant/when only three morphologies (long, wide and diffuse) were significant. †See Figure 1 and text. Abbreviations as in Table 3.

Table 5. Positive Predictive Value of Calcification Morphology for All Coronary Atherosclerotic Lesions According to Patient Age

Age Group (yr)	No. of Pts/ Segments	Calcification Morphology				
		Diffuse	Wide	Long	Spotty	None
<40	16/158	—	—	—	0.33	0.66
≤40 to <50	47/464	1.00	0.90	0.83	0.45	0.12
≤50 to <60	57/563	0.96	0.86	0.78	0.55	0.15
≤60 to <70	78/764	0.95	0.75	0.91	0.61	0.23
≤70	53/521	0.96	0.88	0.90	0.69	0.23
All	251/2,470	0.96	0.84	0.87	0.59	0.17

Pts = patients.

cation, and 56 (53%) of 105 eccentric lesions were associated either diffuse or long calcifications (Fig. 4). Of the 314 segments with significant stenosis, 77 segments (25%) showed no detectable calcification. Of the 524 segments with mild stenosis, 236 (45%) showed no detectable calcification. Calcification was detected by EBCT in 131 (8%) of 1,632 angiographically normal segments.

Discussion

To our knowledge, the present study is the first site by site morphologic comparison of coronary calcification demonstrated by EBCT and angiographically defined coronary stenosis. Detection of calcification by EBCT was highly useful for site by site prediction of clinically significant stenosis. Morphologic classification of the calcifications improved the PPV for clinically significant stenosis and also correlated with angiographic lesion morphology.

Site by site prediction of coronary stenosis. In a previous study (17) performed in the same patient group as that in the present study, the total coronary calcification score predicted coronary stenosis. The sensitivity, specificity, PPV, NPV and accuracy of the total calcification score were 0.77, 0.86, 0.86, 0.76 and 0.81, respectively. The sensitivity (0.75), specificity (0.81) and accuracy (0.80) of calcification for prediction of significant stenosis was similar in the present study, but the PPV (0.36) was significantly lower ($p < 0.0001$ by chi-square analysis) and the NPV (0.96) significantly higher ($p < 0.0001$). These differences were revealed by the site by site comparison. As in our previous study (17), the prevalence and amount of

Table 6. Positive Predictive Value of Calcification Morphology for Significant Coronary Stenosis According to Patient Age

Age Group (yr)	No. of Pts/ Segments	Calcification Morphology				
		Diffuse	Wide	Long	Spotty	None
<40	16/158	—	—	—	0.33	—
≤40 to <50	47/464	1.00	0.60	0.17	0.09	0.03
≤50 to <60	57/563	0.61	0.43	0.31	0.13	0.04
≤60 to <70	78/764	0.58	0.38	0.36	0.19	0.06
≤70	53/521	0.50	0.29	0.34	0.23	0.06
All	251/2,470	0.56	0.40	0.32	0.18	0.04

Pts = patients.

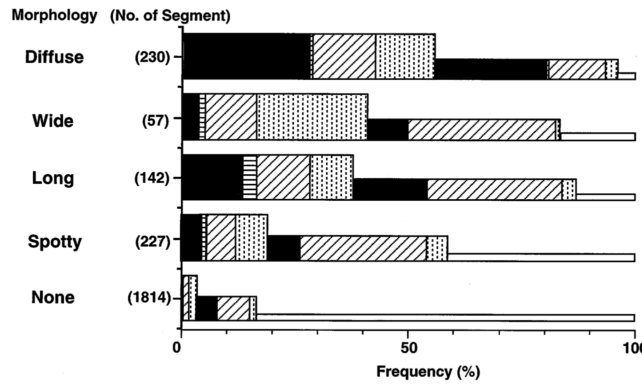
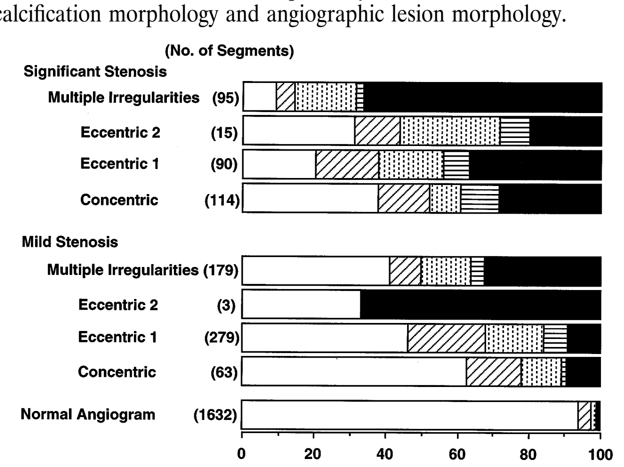


Figure 3. Frequency of various types of angiographically defined coronary stenosis according to the morphologic classification of calcification. Significant stenosis, mild (not significant) stenosis and normal angiographic results are represented as wide, middle and narrow **bars,** respectively. Lesions were classified into multiple irregularities (**solid boxes**), eccentric type 1 (**hatched boxes**), eccentric type 2 (**horizontally striped boxes**) and concentric (**dashed boxes**).

coronary calcification increased with age, even in patients without significant stenosis. These findings may explain why the PPV and sensitivity increased significantly with age for all atherosclerotic lesions. The PPV and sensitivity did not increase with age for significant stenosis. Although the explanation for these discrepancies is unclear, it is possible that it is related to the undetermined role of calcification in the development of lumen narrowing.

Most studies of coronary calcification (6–18) have determined the total calcification score, in which small multifocal calcifications have the same score as large single calcifications, if the total amount of calcification is similar. In the present study, large calcifications were more frequently associated with significant narrowing at the calcified site than with spotty

Figure 4. Frequency of various types of morphologic calcifications in angiographically determined coronary stenosis. Diffuse, wide, long and spotty calcifications are represented by **solid**, **horizontally striped**, **dashed** and **hatched boxes**, respectively. See text for definitions of calcification morphology and angiographic lesion morphology.



calcifications. The total calcification score does not provide information related to the lesion location (17); this limitation can be overcome by a site by site comparative study.

Histopathologic site by site comparisons of calcification and lumen narrowing (21–26) have yielded conflicting results. Simons et al. (21) reported that >97% of noncalcified segments were associated with nonobstructive (<75%) stenosis and that there was no significant stenosis without calcification. However, Mautner et al. (23) reported that calcification was identified by EBCT in only 54% of segments with significant stenosis. The frequency of calcification-free significant stenosis was 25% in the present study. Further investigations will be needed to establish the relation between calcification and degree of lumen narrowing.

Can morphologic classification of calcifications improve predictive value? The PPV differed among morphologic classifications of calcification in the present study. Previous histopathologic studies (21–23,25) have suggested that these differences may be related to differences in the amount of calcification. In the present study, the mean calcified area was significantly greater for long and wide calcifications than for spotty calcification. Diffuse calcification was associated with the greatest mean calcified area, although there was significant overlap in calcified area between diffuse and long or diffuse and wide calcification. These findings suggest that both the morphology and the amount of calcification are important for prediction of stenotic lesions in a calcified area. The amount of calcification appears to be influenced by the lesion location because the coronary artery diameter shows a wide variation depending on the location (proximal or distal), which suggests the potential merit of morphologic evaluation compared with simple quantification of calcification.

The reason for the age-associated alterations in the PPV observed in the present study is unclear. However, these alterations of values appeared to be useful for prediction of stenosis in the clinical setting.

Calcification morphology is correlated with angiographic lesion morphology. Diffuse calcification may indicate the existence of a large amount of atherosclerotic plaque in the vessel wall and was thus associated with significant stenosis, especially with stenosis of multiple irregularities. Wide calcification was more frequently associated with significant stenosis than long calcification, and the frequency of concentric lesions was highest for wide calcifications than for the other morphologic groups ($p < 0.01$ by chi-square analysis). These results suggest that the development of a calcification in the transaxial direction of the vessel tends to result in concentric stenosis. If compensatory enlargement (27) occurs along the entire coronary artery tree, the cross-sectional extent of atheromatous plaque may be more strongly correlated with lumen obstruction than the longitudinal extent. This concept may also be applicable to coronary calcification, and the present findings concerning wide calcification may support this theory.

The calcification morphology differed among lesions classified angiographically. In lesions with significant stenosis, the calcification-free rate was highest in concentric lesions (0.38 for 43 of 114) and lowest in lesions with multiple irregularities (0.12 for 11 of 95). Moreover, the calcification-free rate was lower in eccentric type 1 lesions (0.20 for 18 of 90), with borderline significance ($p = 0.059$ by chi-square analysis) compared with concentric lesions. This difference was significant ($p < 0.05$ by chi-square analysis) for lesions with mild stenosis. Thus, it is possible that the development of calcification influences the direction of the progression of atheromatous plaque.

Study limitations. The possible limitations of the present study are related to the detection of calcification and to the method used to compare EBCT images and angiographic findings. Image acquisition by EBCT is significantly influenced by the partial volume effect (28). The relatively low frequency of calcifications observed in S-7 and S-10 may be explained in part by the small size of these vessels, which could enhance the partial volume effect. To minimize this effect, we used two scans performed in rapid succession (17) and analyzed the scan showing the larger calcified area.

The comparison of EBCT images and angiography was difficult in some cases. Calcification morphology and angiographic lesion morphology were independently determined, as were their locations. If determinations were unclear, EBCT images and angiograms were simultaneously reevaluated by our staff. This reevaluation was performed in 7 of 251 patients and resulted in a revision of the original determination in 2. To confirm the consistence of our review process, we reanalyzed 25 randomly selected patients; no revisions were needed. Thus, it is unlikely that the method used for morphologic classification and location determination affected our results.

Coronary atherosclerosis occurs and develops multifocally, even in the same patient, and it is not surprising that there are multiple severe stenoses in the LAD with trivial lesions in the RCA. Thus, we performed the present study only on a segment to segment basis. It will require further study to investigate how patient characteristics influence the relation between calcification and atherosclerosis. We ignored lesion continuities in our division of the coronary artery tree in some segments. If there was a large calcification from S-4 to S-5, for example, we analyzed the calcification morphology in each segment. This approach may have influenced our results. To overcome this problem, a new method for comparison is needed. In addition, our results may have been influenced by the clinical characteristics of our study patients because the PPVs and NPVs are largely influenced by the prevalence of disease.

Clinical implications. The present study suggests that the morphologic evaluation of calcifications using EBCT is useful for prediction of the presence and location of clinically significant stenosis in patients with suspected coronary artery disease. Furthermore, its validity improved when combined with the results of total calcification score.

Our results also suggest that EBCT study could provide important findings supplementary to those of angiography. Occasionally, there is a question as to the existence of a lesion in the left main coronary artery versus catheter spasm. The findings of no calcification in the left main coronary artery on EBCT images would be extremely useful in that instance to exclude, to a large extent, the possibility of a significant left main coronary lesion. Similar considerations might be applicable to ostial lesions of the RCA.

Acute coronary syndromes frequently result from mild to moderate stenosis (31–33), suggesting that detection and characterization of preclinical coronary stenosis is important. Thus, the ability of EBCT to predict mild stenosis as well as significant lesions may be highly useful in the clinical setting.

There is increasing evidence that calcium formation associated with atherosclerotic disease is an active process (34,35), which suggests a significant relation between the development of calcification and some unknown characteristics of atherosclerotic plaque. The presence of calcification reportedly influences the outcome of catheter interventions (36,37). Thus, combined angiographic and EBCT studies may provide useful information concerning the status of atherosclerotic plaque.

Conclusions. Morphologic evaluation of coronary artery calcification using EBCT improved the predictive power of angiographically defined coronary atherosclerosis. In addition, it predicted, at least in part, the angiographic lesion morphology observed angiographically.

We express special thanks to the staff cardiologists (Sensyu Hifumi, MD and colleagues) and technicians of Kanazawa Cardiovascular Hospital for their assistance in data collection and image analysis.

References

1. Blankenhorn DH, Stern D. Calcification of the coronary arteries. AJR Am J Roentgenol 1959;81:772–7.
2. Eggen DA, Strong JP, McGill HC. Coronary calcification: relationship to clinically significant coronary lesions and race, sex, and topographic distribution. Circulation 1965;32:948–55.
3. McCarthy JH, Palmer FJ. Incidence and significance of coronary artery calcification. Br Heart J 1974;36:499–506.
4. Boyd D, Gould R, Quinn J, Sparks R, Stanley R, Hermannsfeldt W. A proposed dynamic cardiac 3-D densitometer for easy detection and evaluation of heart disease. IEEE Trans Nucl Sci 1979;26:2724–7.
5. Bartel AG, Chen JT, Peter RH, Behar VS, Kong Y, Lester RG. The significance of coronary calcification detected by fluoroscopy. Circulation 1974;49:1247–53.
6. Agatston AS, Janowitz WR, Hindner FJ, Zusmer NR, Viamonte M, Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. J Am Coll Cardiol 1990;15:827–32.
7. Breen JF, Sheedy PF, Schwartz RS, et al. Coronary artery calcification detected with ultrafast CT as an indication of coronary artery disease: work in progress. Radiology 1992;185:435–9.
8. Borman JL, Stanford W, Stenberg RG, et al. Ultrafast computed tomographic detection of coronary artery calcification as an indicator of stenosis. Am J Cardiac Imag 1992;6:191–6.
9. Georgiou D, Budoff M, Kennedy J, et al. The value of ultrafast CT coronary calcification in predicting significant coronary artery disease compared to angiography: a multicenter study [abstract]. Circulation 1993;88 Suppl I:I–639.
10. Fallavollita JA, Brody AS, Bunnell IL, Kumar K, Canty JM Jr. Fast computed tomography detection of coronary calcification in the diagnosis of coronary artery disease: comparison with angiography in patients <50 years old. Circulation 1994;89:285–90.
11. Wong ND, Vo A, Abrahamson D, Tobis JM, Eisenberg H, Detrano RC. Detection of coronary artery calcium by ultrafast computed tomography and its relation to clinical evidence of coronary artery disease. Am J Cardiol 1994;73:223–7.
12. Barbir M, Bowker T, Ludman PF, Mitchell AG, Wood D, Yacoub M. Ultrafast computed tomographic scanning for detection of coronary disease in cardiac transplant recipients. Am J Cardiol 1994;74:941–4.
13. Agatston AS, Janowitz WR, Kaplan G, Gasso J, Hinder F, Viamonte M Jr. Ultrafast computed tomography-detected coronary calcium reflects the angiographic extent of coronary arterial atherosclerosis. Am J Cardiol 1994;74:1272–4.
14. Devries S, Wolkfiel C, Fusman B, et al. Influence of age and gender on the presence of coronary calcium detected by ultrafast computed tomography. J Am Coll Cardiol 1995;25:76–82.
15. Kaufmann RB, Peyser PA, Sheedy PF, Rumberger JA, Schwartz RS. Quantification of coronary artery calcium by electron beam computed tomography for determination of severity of angiographic coronary artery disease in younger patients. J Am Coll Cardiol 1995;25:626–32.
16. Rumberger JA, Sheedy PF, Breen JF, Schwartz RS. Coronary calcium, as determined by electron beam computed tomography, and coronary disease on arteriogram. Effects of patient's sex on diagnosis. Circulation 1995;91: 1363–7.
17. Kajinami K, Seki H, Takekoshi N, Mabuchi H. Noninvasive prediction of coronary atherosclerosis by quantification of coronary artery calcification using electron beam computed tomography: comparison with electrocardiographic and thallium exercise stress test results. J Am Coll Cardiol 1995;26: 1209–21.
18. Budoff MJ, Georgiou D, Brody A, et al. Ultrafast computed tomography as a diagnostic modality in the detection of coronary artery disease. A multicenter study. Circulation 1996;93:898–904.
19. Detrano R, Hsiai T, Wang S, et al. Prognostic value of coronary calcification and angiographic stenoses in patients undergoing coronary angiography. J Am Coll Cardiol 1996;27:285–90.
20. Arad Y, Spadaro LA, Goodman K, et al. Predictive value of electron beam computed tomography of the coronary arteries: 19-months follow-up of 1173 asymptomatic subjects. Circulation 1996;93:1951–3.
21. Simons DB, Schwartz RS, Edwards WD, Sheedy PF, Breen JF, Rumberger JA. Noninvasive definition of anatomic coronary artery disease by ultrafast computed tomographic scanning: a quantitative pathologic comparison study. J Am Coll Cardiol 1992;20:1118–26.
22. Rumberger JA, Schwartz RS, Simons DB, Sheedy PF, Edwards WD, Fitzpatrick LA. Relation of coronary calcium determined by electron beam computed tomography and lumen narrowing determined by autopsy. Am J Cardiol 1994;74:1169–73.
23. Mautner GC, Mautner SL, Froehlich J, et al. Coronary artery calcification: assessment with electron beam CT and histomorphometric correlation. Radiology 1994;192:619–23.
24. Mautner SLC, Mautner GC, Froehlich J, et al. Coronary artery disease: prediction with in vitro electron beam CT. Radiology 1994;192:625–30.
25. Sangiorgi G, Srivasta SS, Staab M, et al. Total coronary calcified volume is highly correlated with total plaque volume: a histologic study of 723 segments [abstract]. J Am Coll Cardiol 1995;25 Suppl A:386A.
26. Rumberger JA, Simons DB, Fitzpatrick LA, Sheedy PF, Schwartz RS. Coronary artery calcium area by electron-beam computed tomography and coronary atherosclerotic plaque area: a histopathologic correlative study. Circulation 1995;92:2157–62.
27. Glagov S, Weisenberg E, Zarins CK, Stankunavicius R, Kolettis GJ. Compensatory enlargement of human atherosclerotic coronary arteries. N Engl J Med 1987;316:1371–5.
28. Kajinami K, Seki H, Takekoshi N, Mabuchi H. Quantification of coronary artery calcification using ultrafast computed tomography: reproducibility of measurements. Coronary Art Dis 1993;4:1103–8.
29. Ambrose JA, Winters SL, Arona RR, et al. Coronary angiographic morphology in myocardial infarction: a link between the pathogenesis of unstable angina and myocardial infarction. J Am Coll Cardiol 1985;6:1233–8.
30. Austen WG, Edwards JE, Frye RL, et al. A reporting system on patients evaluated for coronary artery disease: report of the ad hoc committee for grading of coronary artery disease. Circulation 1975;51 Suppl:5–40.
31. Ambrose JA, Tannenbaum MA, Alexopoulos D, et al. Angiographic progression of coronary artery disease and the development of myocardial infarction. J Am Coll Cardiol 1988;12:56–62.

32. Little WC, Constantinescu M, Applegate RJ, et al. Can coronary angiography predict the site of a subsequent myocardial infarction in patients with mild-to-moderate coronary artery disease? Circulation 1988;78:1157–66.
33. Nobuyoshi M, Tanaka M, Nosaka H, et al. Progression of coronary atherosclerosis: is coronary spasm related to progression? J Am Coll Cardiol 1991;18:904–10.
34. Bostrom K, Watson KE, Horn S, Wortham HC, Herman IM, Demer LL. Bone morphogenic protein expression in human atherosclerotic lesions. J Clin Invest 1993;91:1800–9.
35. Fitzpatrick LA, Severson A, Edwards WD, Ingram RT. Diffuse calcification in human coronary arteries: association of osteopontin with atherosclerosis. J Clin Invest 1994;94:1597–604.
36. Fitzgerald PJ, Ports TA, Yock PG. Contribution of localized calcium deposits to dissection after angioplasty: an observational study using intravascular ultrasound. Circulation 1992;86:64–70.
37. Weiss RM, Berg TD, Thompson BH, Stanford W. Coronary calcium assessment by electron beam tomography forecasts acute complications of angioplasty [abstract]. J Am Coll Cardiol 1996;27 Suppl A:175A–6A.